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3610 Rec'd PCT/PTO 2 8 JUN 2001

FORM PTO 1390 (REV 10-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER 114750.2300	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				U.S. APPLICATION NO. (If known, see 37 CFR 1.5) <b>09/869394</b>	
INTERNATIONAL APPLICATION NO. PCT/EP99/09291		INTERNATIONAL FILING DATES 30 November 1999 (30.11.99)		PRIORITY DATE CLAIMED 28 December 1998 (28.12.98)	
TITLE OF INVENTION SUN PROTECTION PRODUCT WITH MICROPARTICLES ON THE BASIS OF WATER-INSOLUBLE LINEAR POLYGLUCAN					
APPLICANT(S) FOR DO/EO/US BENGES, et al.					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
<ol style="list-style-type: none"><li>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li><li>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li><li>3. <input checked="" type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371 (f)).</li><li>4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).</li><li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371 (c)(2))<ol style="list-style-type: none"><li>a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input type="checkbox"/> has been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li></ol></li><li>6. <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).</li><li>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))<ol style="list-style-type: none"><li>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).</li><li>b. <input type="checkbox"/> have been communicated by the International Bureau.</li><li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li><li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li></ol></li><li>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).</li><li>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).</li><li>10. <input checked="" type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).</li></ol>					
Items 11 to 16 below concern document(s) or information included:					
<ol style="list-style-type: none"><li>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li><li>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 &amp; 3.31 is included.</li><li>13. <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment. <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment.</li><li>14. <input type="checkbox"/> A substitute specification.</li><li>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</li><li>16. <input checked="" type="checkbox"/> Other items or information: International Search Report</li></ol>					

JC-18 Rec'd PCT/PTO 2 8 JUN 2001

U.S. APPLICATION NO. (if known, see 37 CFR 1.51) <div style="font-size: 2em; font-weight: bold; text-align: center;">09/869394</div>		INTERNATIONAL APPLICATION NO. PCT/EP99/09291		ATTORNEY'S DOCKET NUMBER 114750.2300																																																												
17. <input checked="" type="checkbox"/> The following fees are submitted: <b>BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) – (5)):</b> <div style="margin-left: 20px;"><input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO .....\$1000.00 <input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO ..... \$860.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$710.00 <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) ..... \$690.00 <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) ..... \$100.00</div> <div style="text-align: right; margin-right: 20px;"><b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b> \$ 860 00</div> <div style="margin-top: 10px;">Surcharge of \$ _____ for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).</div>				<b>CALCULATIONS</b> PTO USE ONLY <div style="border: 1px solid black; height: 150px; margin-top: 5px;"></div>																																																												
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a. <input checked="" type="checkbox"/> A check in the amount of \$ 860.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 50-0436 in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required or credit any overpayment to my Deposit Account No. 50-0436. A duplicate copy of this sheet is enclosed.																																																																
<b>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.</b>																																																																
SEND ALL CORRESPONDENCE TO: <div style="margin-top: 20px;"><div style="display: flex; justify-content: space-between;"><div>PEPPER HAMILTON LLP Hamilton Square 600 14<sup>th</sup> Street, NW Washington, D.C. 20005-2004</div><div style="text-align: right;"><div style="font-size: 1.5em; font-weight: bold; margin-bottom: 5px;">Signature</div><div style="font-size: 1.2em; margin-bottom: 5px;">Gilberto M. Villacorta, Ph.D.</div><div style="font-size: 1.2em; margin-bottom: 5px;">NAME</div><div style="font-size: 1.2em; margin-bottom: 5px;">34,038</div><div style="font-size: 1.2em; margin-bottom: 5px;">REGISTRATION NUMBER</div><div style="font-size: 1.2em; margin-bottom: 5px;">DATE: Jan 28, 2001</div></div></div></div>																																																																

Docket No.: 114750.2300

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: BENGS, et al.

Art Unit: Not Yet Assigned

Serial No.: Not Yet Assigned

Examiner: Not Yet Assigned

Filed: June 28, 2001

For: SUN PROTECTION PRODUCT WITH MICROPARTICLES ON THE BASIS OF  
WATER-INSOLUBLE LINEAR POLYGLUCAN

**PRELIMINARY AMENDMENT**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to examination on the merits, please amend the above-referenced application as follows:

**IN THE CLAIMS**

Please amend the claims as follows:

Please cancel claims 1-14 without prejudice or disclaimer.

Please add the following new claims:

--15. A sun protection product which comprises spherical microparticles wherein the spherical microparticles comprise at least one water-insoluble linear polyglucan having a degree of branching of less than 0.5% in the 6-position.

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**PATENT**

16. The sun protection product as claimed in claim 15, wherein the water-insoluble linear polyglucan has a degree of branching of at most 2% in the other positions.
17. The sun protection product as claimed in claim 15, wherein the microparticles have an average diameter of from 1 nm to 100 µm.
18. The sun protection product as claimed in claim 15, wherein the depth of irregularities on the surface of the microparticles is at most 20% of the average diameter of the microparticles.
19. The sun protection product as claimed in claim 15, wherein the microparticles are present in the sun protection product in an amount of from 05.% to 70% by weight, based on the total weight of the sun protection product.
20. The sun protection product as claimed in claim 15, wherein the water-insoluble linear polyglucan is selected from the group consisting of poly-1,4-α-D-glucan, poly-1,3-β-D-glucan, and a mixture thereof.
21. The sun protection product as claimed in claim 15, wherein the water-insoluble linear polyglucan is produced by a biotechnological method.
22. The sun protection product as claimed in claim 15, wherein the water-insoluble linear polyglucan is produced biocatalytically.
23. The sun protection product as claimed in claim 15, wherein the microparticles further comprise branched polysaccharides and further polymers.
24. The sun protection product as claimed in claim 15, wherein the microparticles comprise at least 70% water-insoluble linear polyglucan based on the total content of polyglucan in the microparticles.

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**PATENT**

25. The sun protection product as claims in claim 15, wherein the microparticles comprise 100% of the at least one water-insoluble linear polyglucan.
26. The sun protection product as claimed in claim 15, wherein the microparticles are dispersed in the sun protection product and have a dispersity in the range of from 1.0 to 10.0.
27. A method of making a sun protection product comprising preparing spherical microparticles comprising at least one water-insoluble polyglucan having a degree of branching of less than 0.5% in the 6-position.
28. The method as claimed in claim 27, wherein the microparticles have an average diameter of from 1 nm to 100  $\mu\text{m}$ .
29. The method as claimed in claim 27, wherein the microparticles microparticles are dispersed in the sun protection product and have a dispersity in the range of from 1.0 to 10.0.
30. The method as claimed in claim 27, wherein the water-insoluble linear polyglucan is selected from the group consisting of poly-1,4- $\alpha$ -D-glucan, poly-1,3- $\beta$ -D-glucan, or a mixture thereof.
31. A method of sun protection comprising applying a sun protection product which comprises spherical microparticles wherein the spherical microparticles comprise at least one water-insoluble linear polyglucan having a degree of branching of less than 0.5% in the 6-position.
32. The method as claimed in claim 31, wherein the microparticles have an average diameter of from 1 nm to 100  $\mu\text{m}$ .
33. The method as claimed in claim 31, wherein the microparticles are dispersed in the sun protection product and have a dispersity in the range of from 1.0 to 10.0.

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**PATENT**

34. The method as claimed in claim 31, wherein the water-insoluble linear polyglucan is selected from the group consisting of poly-1,4- $\alpha$ -D-glucan, poly-1,3- $\beta$ -D-glucan, or a mixture thereof.--

**IN THE ABSTRACT**

Please enter the Abstract attached hereto on a separate page.

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**PATENT**

**REMARKS**

The claims have been amended to be in better form for U.S. practice. Further, an Abstract on a separate page has been added. Upon entry of these amendments, claims 15-34 will be pending.

Entry of the above amendments prior to examination of the above-referenced application is respectfully requested

**AUTHORIZATION**

The Commissioner is hereby authorized to charge any fees which may be required for this Amendment, or credit any overpayment to Deposit Account No. 50-0436.

Respectfully Submitted,  
PEPPER HAMILTON LLP



Gilberto M. Villacorta, Ph.D.  
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Date: June 28, 2001

Docket No.: 114750.2300

**PATENT**

**ABSTRACT**

The present invention relates to a sun protection product which contains microparticles as the active agent, wherein the microparticles comprise water-insoluble linear polyglucan.

DC: #189868 v1 (42\$401!.DOC) 114750-2300



WO 00/38622

Sun protection product with microparticles on the basis  
of water-insoluble linear polyglucan

Description

5

The present invention relates to a sun protection product with microparticles on the basis of water-insoluble linear polyglucan which, on the one hand, ensures good UV protection and appears transparent upon application.

10

Known sun protection products comprise inter alia pigments, such as, for example, titanium dioxide and zinc oxide as such or in the form of "micronized particles" as light protection filters.

15

From a cosmetics viewpoint, these pigments have the disadvantage that they whiten, i.e. make the skin appear white in colour.

20

As a compromise for reducing the whitening to a tolerable degree and nevertheless achieving an acceptable UV protection, these pigments are usually used with a comparatively small particle size between 10 and 100 nm (A. Schrader, M. Rohr "Auffälligkeiten bei der Entwicklung und Prüfung von mikropigmenthaltigen Sonnenschutzformulierungen [Unusual features in the development and testing of sun protection formulations containing micropigments]" SÖFW Journal, 124, pages 478-487, 8/98).

25

30

In addition, titanium dioxide is to be viewed critically from a health viewpoint. In a study using titanium dioxide which had been extracted from sun protection products, it was observed upon irradiation with sunlight that titanium dioxide is able to catalyze photooxidation and damages bacterial DNA (CTFA/TRN Volume 12, No. 3, page 5 (1998) with reference to FEBS Letters, 418, 87-90, 1997).

35

A light-protecting action is also known for individual polysaccharides. For example, a light-protecting action has been described for poly- $\beta$ -1,3-glucans (H. Eggensperger, M. Wilker, "Multiaktiv wirksame Polysaccharide Teil I-Pilzextrakte und Teil II-Pflanzliche Polysaccharide [Multiactive polysaccharides part I-fungus extracts and part II-vegetable polysaccharides]" in SÖFW Journal, 123, 8/97, pages 542-546 and 12/97, pages 838-842).

Poly- $\beta$ -1,3-glucans which can be obtained from yeasts have a linear structure with a small proportion of  $\beta$ -1,6 branching.

It has also been proposed to use glycogen (a highly branched poly-1,4- $\alpha$ -glucan with branching in the 6-position) obtained biotechnologically or from marine molluscs for sun protection products (M. Pauly, G. Pauly "New Polysaccharides Interest in Care Cosmetology" IN-COSMETICS 1997, Conference Proceedings, pages 417-444, Verlag für chemische Industrie, H. Ziolkowsky GmbH, 1998).

EP-B-0 487 000 proposes the use of a cosmetic composition in the form of an emulsion having 15 to 40% by weight of an enzymatically debranched starch in sun protection products, where the enzymatically degraded starch is a linear poly-1,4- $\alpha$ -glucan having 15 to 65 anhydroglucose units. However, there is no reference to a potential light protection action of the enzymatically debranched starch used therein; instead, it is used as an emulsifying auxiliary.

In view of the risks of intensive UV exposure, there is a growing need for suitable sun protection filters which not only offer reliable protection, but also do not impair the external appearance and are thus also suitable for daily use.





- 5 -

For the present invention, spherical microparticles are to be understood as meaning microparticles which have a virtually spherical shape. If a sphere is described by axes of identical length which start from a common  
5 origin and are directed into space and define the radius of the sphere in all spatial directions, the lengths of the axes may deviate from an ideal spherical state by from 1% to 40% for the spherical particles. The deviation is preferably 25% or less, particularly  
10 preferably 15% or less.

The spherical particles have a regular surface which can be compared macroscopically with a raspberry, where the depth of irregularities on the particle surface,  
15 such as recesses or indentations, is at most 20%, preferably 10%, of the average diameter of the spherical microparticles.

The specific surface area of the microparticles is  
20 generally from 1 m<sup>2</sup>/g to 100 m<sup>2</sup>/g, preferably 1.5 m<sup>2</sup>/g to 20 m<sup>2</sup>/g and particularly preferably 3 m<sup>2</sup>/g to 10 m<sup>2</sup>/g.

Furthermore, the particles according to the invention preferably have a dispersity  $D = \text{weight-average diameter } (d_w) / \text{number-average diameter } (d_n)$  of from 1.0  
25 to 10.0, in particular from 1.5 to 5.0 and particularly preferably from 2.0 to 3.0.

The averages used herein are defined as follows:

30  $d_n = \text{sum of } n_i \times d_i / \text{sum of } n_i = \text{number-average}$   
 $d_w = \text{sum of } n_i \times d_i^2 / \text{sum of } n_i \times d_i = \text{weight-average}$   
 $n_i = \text{number of particles with diameter } d_i,$   
 $d_i = \text{a particular diameter,}$   
 $i = \text{serial parameter.}$

35

In this connection, the term weight indicates a weighted average, as a result of which the larger diameters are given greater importance.

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The microparticles used according to the invention may also have been subjected to a surface modification by, for example, derivatizing functional groups, such as hydroxyl groups, of the polyglucans.

5

For the purposes of the present invention, linear water-insoluble polyglucans are polysaccharides built up from glucans as monomeric building blocks such that the individual building blocks are always linked together in the same way. Each basic unit or building block defined in this way has exactly two linkages, each to one other monomer. The only exceptions to this are the two base units which form the start and the end of the polysaccharide. These have only one linkage to a further monomer and form the end-groups of the linear polyglucan.

If the base unit has three or more linkages, then this is referred to as branching. In this context, the number of hydroxyl groups per 100 base units which are not involved in constructing the linear polymer backbone and form the branches gives the "degree of branching". According to the invention, the linear water-insoluble polyglucans have a degree of branching of at most 8%, i.e. they have a maximum of 8 branches and 100 base units. The degree of branching is preferably less than 4% and in particular at most 2.5%.

Particular preference is given to polyglucans whose degree of branching in the 6-position is less than 4%, preferably at most 2% and in particular at most 0.5%, and is preferably in each case at most 2% and in particular 1% in the other positions, e.g. in the 2- or 3-position. Particular preference is also given to polyglucans with a degree of branching in the 6-position of less than 0.5%.

Of particular suitability for the invention are polyglucans which have no branches or whose degree of

- 7 -

branching is so minimal that it is no longer detectable by traditional methods.

5 Examples of preferred water-insoluble linear polyglucans are linear poly-D-glucans, the nature of the linkage being unimportant, provided there is linearity within the meaning of the invention. Examples are poly-alpha-D-glucans, in particular poly-1,4-alpha-D-glucan, and poly-1,3-beta-D-glucans, particular  
10 preference being given to poly-1,4- $\alpha$ -D-glucan.

For the present invention, the prefixes "alpha", "beta" or "D" refer solely to the linkages forming the polymer backbone and not to the branches.

15

For the present invention, the term "water-insoluble polyglucan" is to be understood as meaning compounds which, according to the definition of the German Pharmacopoeia (DAB = Deutsches Arzneimittelbuch, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, Govi-Verlag, Frankfurt, [lacuna] edition, 1987), fall into the categories "slightly soluble", "sparingly soluble", "very sparingly soluble" and "virtually insoluble" compounds, corresponding to classes 4 to 7.

25

In the case of the polyglucans used according to the invention, this means that at least 98% of the amount used, in particular at least 99.5%, are insoluble in water under standard conditions ( $T = 25^{\circ}\text{C} \pm 20\%$ ,  
30  $p = 101325 \text{ Pascal} \pm 20\%$ ) (corresponding to classes 4 and 5, respectively).

For the present invention, preference is given to sparingly soluble to virtually insoluble compounds, in particular very sparingly soluble to virtually  
35 insoluble compounds.

"Very sparingly soluble" corresponding to class 6 can be illustrated by the following protocol:

- 8 -

One gram of the polyglucan to be investigated is heated in 1 l of deionized water to 130°C at a pressure of 1 bar. The solution which forms only remains stable briefly for a few minutes. Upon cooling under standard  
5 conditions, the substance precipitates out again. After cooling to room temperature and separation by means of centrifugation, at least 66% of the amount used can be recovered, taking into account experimental losses.

10 The polyglucans used according to the invention may be of any origin provided the conditions given above with regard to the terms "linear" and "water-insoluble" are met.

15 They may have been obtained naturally or by biotechnology methods.

For example, they may be obtained from natural vegetable or animal sources by isolation and/or  
20 purification.

It is also possible to use sources which have been manipulated genetically such that they contain a higher proportion of unbranched or comparatively slightly branched polyglucans than the unmanipulated source.

25 They may have been prepared from non-linear polyglucans by enzymatic or chemical debranching.

In this connection, non-linear polyglucans which contain branches may be treated with an enzyme such  
30 that cleavage of the branches arises, leaving, following removal of the branches, linear polyglucans. These enzymes may, for example, be amylases, isoamylases, gluconohydrolases, pullulanases or cyclomaltodextrin glucanotransferases.

35 Biotechnology methods include biocatalytic, including biotransformation, or fermentation processes.



- 9 -

Linear polyglucans prepared by biocatalysis (including: biotransformation) for the purposes of this invention means that the linear polyglucan is prepared by catalytic reaction of monomeric basic building blocks  
5 such as oligomeric saccharides, e.g. of monosaccharides and/or disaccharides, using a biocatalyst, usually an enzyme, under suitable conditions. In this connection, reference is also made to "in vitro biocatalysis".

10 Linear polyglucans from fermentations are, within the language usage of the invention, linear polyglucans which are obtained by fermentation processes using naturally occurring organisms, such as fungi, algae, bacilli, bacteria or protists or using non-naturally  
15 occurring organisms, but using natural organisms modified by genetic methods of the general definition, such as fungi, algae, bacilli, bacteria or protists, or which can be obtained with the insertion and assistance of fermentation processes. Reference is also made in  
20 this connection to "in vivo biocatalysis".

Examples of such microorganisms are *Pichiapastoris*, *Trichoderma reesei*, *Staphylococcus carnosus*, *Escherichia coli*, *Aspergillus niger*.

25

Advantageous processes for the biotechnology production are described, for example, in WO 95/31553 or the previously unpublished German patent application from the applicant with the official file reference  
30 198 27 978.5.

According to WO 95/31553, amylosucrases are used for the preparation of linear water-insoluble polyglucans, such as poly-1,4- $\alpha$ -D-glucan, by means of a biocatalytic  
35 process. Further suitable enzymes are polysaccharide synthases, starch synthases, glycol transferases, 1,4- $\alpha$ -D-glucan transferases, glycogen synthases or phosphorylases.

- 10 -

It is also possible to use modified water-insoluble linear polyglucans, it being possible for the polyglucans to have been chemically modified, for example by esterification and/or etherification in one  
5 or more positions which are not involved in the linear linkage. In the case of the preferred 1,4 linked polyglucans, the modification can take place in the 2-, 3- and/or 6-position.

10 For the purposes of the invention, modification means that the hydroxyl groups present which are not involved in the linkage are chemically changed. This excludes a ring opening of the glucan units, as occurs, for example, during oxidative carboxylation or hydrolysis.  
15 Measures for such modifications are sufficiently known to the person skilled in the art.

Thus, linear polyglucans, such as, for example, pullulans, which are per se water-soluble, can be made  
20 water-insoluble by modification.

For the present invention, use is preferably made of water-insoluble linear polyglucans which have been prepared in a biotechnology process, in particular in a  
25 biocatalytic or a fermentation process.

In contrast to polyglucans which are isolated from natural sources, such as plants, the linear water-insoluble polyglucans obtained here have a particularly  
30 homogeneous property profile, e.g. with regard to the molecular weight distribution, they contain no, or at worst only very small amounts, of undesired byproducts, which have to be separated off at great expense or could trigger allergic reactions, and can be reproduced  
35 in a precisely specified manner in a simple way.

In particular, biotechnology methods may be used to obtain water-insoluble linear polyglucans, such as, for example, the preferred poly-1,4- $\alpha$ -D-glucans which do

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not contain branches or whose degree of branching is below the detection limit of traditional analytical methods.

- 5 In addition, the polyglucans can be used in the form of "alpha-amylase-resistant polyglucans", as are described using the example of poly-1,4- $\alpha$ -D-glucan in the previously unpublished German patent application with an earlier priority date and having the official file  
10 reference 198 30 618.0 from the applicant.

Alpha-amylase-resistant polyglucans can be obtained by preparing a suspension or dispersion of water-insoluble polyglucans and water, heating the suspension or  
15 dispersion to a temperature in the range from 50 to 100°C, allowing the resulting paste-like mixture to cool to a temperature in the range from 50°C down to the freezing point, preferably 35 to 15°C, 27 to 22°C, 16 to 0°C or 6 to 2°C, over a period of from 1 to 72 h,  
20 preferably 1 to 36 h and in particular 15 to 30 h and retrograding the paste-like mixture at a temperature lower than the temperature of the heated paste-like mixture in a temperature range from 90 to 4°C, and, if desired, drying or dewatering the resulting product.

25 The polyglucan can also be used as thermoplastic polyglucan obtainable by melting on linear water-insoluble polyglucan and adding at least 20% by weight, preferably at least 30% by weight, of a softener such  
30 as sorbitol, glycerol, condensation products thereof and oligomers, DMSO, succinic acid, citric acid monohydrate, malic acid, tartaric acid, etc. at about 170°C.

35 A description of suitable measures and properties of thermoplastic polyglucans using the example of the preferred linear water-insoluble poly-1,4- $\alpha$ -D-glucan is given in the previously unpublished German patent application which has an earlier priority date and the

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official file reference 198 52 826, to which express reference is made here.

5 The molecular weights  $M_w$  (weight-average, determined by means of gel permeation chromatography relative to calibration with a pullulan standard) of the linear polyglucans used according to the invention can vary within a wide range from  $0.75 \times 10^2$  g/mol to  $10^7$  g/mol. The molecular weight  $M_w$  is preferably in a range from  
10  $10^3$  g/mol to  $10^6$  g/mol and particularly preferably from  $10^3$  g/mol to  $10^5$  g/mol. A further advantageous range is from  $2 \times 10^3$  to  $8 \times 10^3$ . Corresponding ranges apply to the preferably used poly-1,4-D-glucan.

15 The molecular weight distribution or polydispersity  $M_w/M_n$  may likewise vary within wide ranges depending on the polyglucan preparation process. Preferred values are from 1.01 to 50, in particular from 1.01 to 15. Particular preference is given to polyglucans with low  
20 dispersity values, such as e.g. 1.01 - 2.5. The polydispersity increases with a bimodal distribution of the molecular weights.

For the preparation of the microparticles it is  
25 possible to use a single polyglucan, in particular poly-1,4-D-glucan and very particularly poly-1,4- $\alpha$ -D-glucan or mixtures of two or more representatives.

30 In a further embodiment, a water-insoluble branched polysaccharide, preferably a polyglucan, in particular a poly-1,4- $\alpha$ -D-glucan or a poly-1,3- $\beta$ -D-glucan, can be added.

It is also possible to add mixtures of two or more branched polysaccharides.

35

The branched polysaccharides can be of any origin. In this connection, reference is made to the explanations regarding this for the linear water-insoluble polyglucans. Preferred sources are starch and starch

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analog, such as glycogen. If required, the proportion of linear structures in the branched polysaccharides can be increased by suitable enrichment methods.

- 5 For the insolubility in water, the same data apply as for the linear water-insoluble polyglucan, the molecular weight can also be higher for the branched polysaccharides, e.g. values up to, preferably,  $10^9$  g/mol and above.

10

It is also possible to admix other polymers, in particular biocompatible or biodegradable polymers. Here, the amount of the other polymer(s) which is/are admixed, without the spherical shape and/or other  
15 properties of the microparticles to be prepared being changed, is always dependent on the polymer added.

To ensure the desired properties of the microparticles, the proportion of linear water-insoluble polyglucan  
20 should be at least 70% by weight, in particular 80% by weight and preferably 90% by weight, based on the total content of linear water-insoluble polyglucan including optionally branched polysaccharide and optionally further polymers.

25

According to a particularly preferred embodiment, the microparticles consist to an extent of 100% by weight of linear water-insoluble polyglucan, in particular linear water-insoluble poly-1,4- $\alpha$ -D-glucan which has  
30 preferably been obtained biocatalytically.

Examples of processes for the preparation of the microparticles are, for example, precipitation processes or spray-drying processes.

35

The spherical microparticles can be prepared by dissolving the water-insoluble linear polyglucan or a mixture of two or more thereof and optionally further polymers in a solvent, e.g. DMSO, introducing the

solution into a precipitating agent, e.g. water, preferably at a temperature of from 20°C to 60°C, if required cooling the solution to a temperature of from -10°C to +10°C and separating off the particles formed in the process.

Here, the dissolution operation of the polyglucan used as starting material can be carried out at room temperature or at higher temperatures.

10 The concentration of linear water-insoluble polyglucan including optionally branched polysaccharide and further polymers in the solvent can vary within wide limits according to requirement. Preferably, it is in a range from 0.02 g/ml to 1.0 g/ml, in particular from 15 0.05 g/ml to 0.8 g/ml and particularly preferably from 0.3 g/ml to 0.6 g/ml.

Examples of precipitating agents are water, dichloromethane, a mixture of water and 20 dichloromethane, and mixtures of water and alcohols such as methanol, ethanol, isopropanol, particular preference being given to water and to a mixture of water and dichloromethane.

25 The ratio of solvent to precipitating agent is preferably chosen in a range from 1 : 1000 to 1 : 4 (part of solvent/parts of precipitating agent), preferably 1 : 100 to 1 : 10 and in particular 1 : 70 to 1 : 30.

30 It is generally unimportant here in which order the solvent and the precipitating agent are combined, e.g. whether the precipitating agent is added to the solvent or vice versa.

35 However, it is important that rapid thorough mixing is  
ensured.

The precipitating process can be carried out relatively slowly at low temperature overnight.

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It can be influenced and controlled by varying the temperature and the precipitating agent.

If cooling is carried out, it must be ensured that the mixture of solvent and precipitating agent remains  
5 liquid and does not solidify.

By co-using suitable additives, it is possible to influence the properties of the microparticles, such as size, surface structure, porosity, etc. and the way in  
10 which the process is carried out.

Suitable additives are, for example, surface-active substances, such as sodium dodecyl sulfate, N-methylgluconamide, polysorbates (e.g. Tween (registered  
15 trademark)), alkylpolyglycol ethers, ethylene oxide-propylene oxide block polymers (e.g. Pluronic (registered trademark)), alkylpolyglycol ether sulfates, generally alkyl sulfates and fatty acid glycol esters, and sugars, such as, for example,  
20 fructose, sucrose, glucose, water-soluble cellulose or hot-water-soluble poly-alpha-D-glucan, such as, for example, natural or chemically modified starches, poly-alpha-D-glucans obtained from these starches, and starch-analogous compounds.

25 These additives are usually added to the precipitating agent. The amount used depends on the individual case in question and the desired particle properties, the determination of the advantageous amount in each case  
30 being known to the person skilled in the art.

By adding water-soluble cellulose derivatives to the precipitating agent, it is possible to obtain microparticles having a particularly smooth surface,  
35 the depth of the irregularities on the surface of the microparticles generally being at most 10% of the average diameter.

Examples of water-soluble cellulose derivatives are cellulose esters and cellulose ethers, mixed forms

10

25

30

35

For this purpose, it is possible to use the same poly-alpha-D-glucan compounds as have been mentioned in connection with the linear water-insoluble polyglucan.





"cold-water-soluble" starches are more readily soluble under these conditions.

The hot-water-soluble starches are characterized in particular by the fact that, upon heating under autogenous pressure, e.g. in an autoclave, to a temperature in the range from about 100 to about 160°C, they form solutions, the temperature in each case depending on the type of starch.

10 For example, potato starch can be boiled at about 100°C until dissolution is complete, while corn starch requires a temperature of about 125°C.

15 For the process according to the invention, the hot-water-soluble poly-alpha-D-glucans are preferably added to the precipitating agent in maximum concentration, i.e. a saturated solution is prepared.

Further suitable ranges are from more than 0.001% by weight to 10% by weight, preferably from 0.01 to 2% by weight and in particular from 0.05% by weight to 0.5% by weight, based on the amount of precipitating agent used.

25 In the case of thermoplastic polyglucan, the additives  
may be incorporated into the thermoplastic mixture in  
an advantageous manner as a plasticizer or in addition  
to the plasticizers, such that a dry powder mixture is  
present which can then be processed to the  
30 microparticles, it also being possible for the  
formation process of the microparticles to be carried  
out in the final formulation with incorporation of the  
thermoplastic polyglucans.

35 A detailed description of the microparticles used here, their preparation and the water-insoluble linear polyglucans which can be used therefor is given in the German patent applications of the applicant which are previously unpublished but which have an earlier

In addition, the microparticles used according to the invention are characterized by high biocompatibility. For the biocompatibility of the microparticles used according to the invention, the nature-identical character of the water-insoluble linear polyglucans, and of their degradation products, used for the preparation, in particular, is of great importance.

20      **Example 1**

35

Assessment of a sun protection product comprising microparticles as in Example 1





Patent claims

1. A sun protection product which comprises, as essential constituent, spherical microparticles which consist entirely or partially of at least one water-insoluble linear polyglucan.
2. The sun protection product as claimed in claim 1, wherein the spherical microparticles have an average diameter of from 1 nm to 100  $\mu$ m.
3. The sun protection product as claimed in claim 1 or 2, wherein the depth of irregularities on the particle surface is at most 20% of the average diameter of the spherical microparticles.
4. The sun protection product as claimed in any of the preceding claims, wherein the microparticles are present in the sun protection product in an amount of from 0.5 to 70% by weight, based on the total weight of the sun protection product.
5. The sun protection product as claimed in any of the preceding claims, wherein the at least one water-insoluble polyglucan is poly-1,4- $\alpha$ -D-glucan and/or poly-1,3- $\beta$ -D-glucan, in particular poly-1,4- $\alpha$ -D-glucan.
6. The sun protection product as claimed in any of the preceding claims, wherein the at least one water-insoluble linear polyglucan has been obtained by a biotechnology method.
7. The sun protection product as claimed in any of the preceding claims, wherein the at least one water-insoluble polyglucan has been produced biocatalytically.

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8. The sun protection product as claimed in any of the preceding claims, wherein the proportion of water-insoluble linear polyglucan in the microparticles is at least 70%, based on the total content of polyglucan including optionally branched polysaccharide and further polymers.  
5
9. The sun protection product as claimed in any of the preceding claims, wherein the microparticles consist to an extent of 100% of at least one water-insoluble linear polyglucan.  
10
10. The sun protection product as claimed in any of the preceding claims, wherein the polyglucan has a degree of branching of at most 8%.  
15
11. The sun protection product as claimed in any of the preceding claims, wherein the polyglucan has a degree of branching of less than 4% in the 6-position, and a degree of branching of at most 2% in the other positions.  
20
12. The sun protection product as claimed in any of the preceding claims, wherein the polyglucan has a degree of branching of less than 0.5% in the 6-position.  
25
13. The sun protection product as claimed in any of the preceding claims, wherein the water-insoluble linear polyglucan is poly-1,4- $\alpha$ -D-glucan which has been produced biotechnologically, in particular biocatalytically.  
30
14. The use of particles which contain at least one water-insoluble linear polyglucan for the preparation of a sun protection product.  
35





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10 Rec'd PCT/INT 25 FEB 2002

Docket No.: 114750.2300

## **DECLARATION AND POWER OF ATTORNEY**

As below named inventor(s), I/We hereby declare that:

My residence, post office and citizenship are as stated below next to my name,

I/We believe I/We am/are the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter claimed and for which a patent is sought on the invention entitled **SUN PROTECTION PRODUCT WITH MICROPARTICLES ON THE BASIS OF WATER-INSOLUBLE LINEAR POLYGLUCAN**, the specification of which [ ] is attached hereto OR [X] was filed on June 28, 2001, as Application Serial No. 09/869,394, and was amended on June 28, 2001 (if applicable).

I/We hereby state that I/We have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I/We acknowledge the duty to disclose information which is known to me to be material to patentability in accordance with Title 37, Code of Federal Regulations, Section 1.56(a).

I/We hereby claim foreign priority benefits under Title 35, United States Code, Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

<b>Prior Foreign Application(s):</b>			<b>Priority Claimed</b>	
<b><u>Number</u></b>	<b><u>Country</u></b>	<b><u>Day/Month/Year filed</u></b>	<b><u>Yes</u></b>	<b><u>No</u></b>
198 60 368.1	Germany	December 28, 1998	X	
PCT/EP99/09291	WO	November 30, 1999	X	

I/We hereby claim the benefit under 35 USC Section 119(e) of any United States provisional application(s) listed below.

**Prior Provisional Application(s):**  
**Application Number**      **Filing Date**

I/We hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I/we acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

**Prior U. S. Application(s):**  
**Serial No.**                      **Filing Date**                      **Status: Patented, Pending, Abandoned**

I/We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Docket No.: 114750.2300

The undersigned hereby grant(s) the firm of PEPPER HAMILTON LLP the power to insert on this Declaration any further identification, including the application number and filing date, which may be necessary or desirable in order to comply with the rules of the United States Patent and Trademark Office for recordation of this document

I/We hereby appoint the following attorney(s) and/or agent(s):

Robert A. Koons, Jr.	Reg. No. <u>32,474</u>	Leo J. Jennings	Reg. No. <u>32,902</u>
Gilberto M. Villacorta, Ph.D.	Reg. No. <u>34,038</u>	Corinne M. Pouliquen	Reg. No. <u>35,753</u>
Kenneth J. Sheehan	Reg. No. <u>36,270</u>	Jean C. Edwards	Reg. No. <u>41,728</u>
Christopher J. Kay, Ph.D.	Reg. No. <u>44,820</u>	Edna Vassilovski	Reg. No. <u>42,198</u>
Paul D. Roath, Ph.D.	Reg. No. <u>45,045</u>	James M. Singer	Reg. No. <u>45,111</u>
Thor B. Nielsen, Ph.D.	Reg. No. <u>45,528</u>	Matthew P. McWilliams	Reg. No. <u>46,922</u>
Sean A. Pryor	Reg. No. <u>48,103</u>	Dawn Sims	Reg. No. <u>47,090</u>

with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and all future correspondence should be addressed to the address at the aforementioned customer number. with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith, and all future correspondence should be addressed to:

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DC: #191549 v1 43ST01! WPD 114750-2300

10 Rec'd PCT/PTO 25 FEB 2002

Docket No.: 114750.2300

**DECLARATION AND POWER OF ATTORNEY**

As below named inventor(s), I/We hereby declare that:

My residence, post office and citizenship are as stated below next to my name,

I/We believe I/We am/are the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter claimed and for which a patent is sought on the invention entitled **SUN PROTECTION PRODUCT WITH MICROPARTICLES ON THE BASIS OF WATER-INSOLUBLE LINEAR POLYGLUCAN**, the specification of which [ ] is attached hereto OR [X] was filed on June 28, 2001, as Application Serial No. 09/869,394, and was amended on June 28, 2001 (if applicable).

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I/We hereby claim foreign priority benefits under Title 35, United States Code, Section 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

**Prior Foreign Application(s):**

<u>Number</u>	<u>Country</u>	<u>Day/Month/Year filed</u>	<u>Priority Claimed</u>	
			<u>Yes</u>	<u>No</u>
198 60 368.1	Germany	December 28, 1998	X	
PCT/EP99/09291	WO	November 30, 1999	X	

I/We hereby claim the benefit under 35 USC Section 119(e) of any United States provisional application(s) listed below.

**Prior Provisional Application(s):**

<u>Application Number</u>	<u>Filing Date</u>
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I/We hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I/we acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56(a) which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

**Prior U. S. Application(s):**

<u>Serial No.</u>	<u>Filing Date</u>	<u>Status: Patented, Pending, Abandoned</u>
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I/We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

**Docket No.: 114750.2300**

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I/We hereby appoint the following attorney(s) and/or agent(s):

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Sean A. Pryor	Reg. No. 48,103	Dawn Sims	Reg. No. 47,090

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